Spontaneous Splenic Rupture in Infectious Mononucleosis: A Review

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Spontaneous rupture of the spleen is a rare complication of infectious mononucleosis (IM) occurring in 0.1-0.5 percent of patients with proven IM [1]. Although splenectomy has been advocated as the definitive therapy in the past, numerous recent reports have documented favorable outcomes with non-operative management. A review of the literature suggests that non-operative management can be successful if appropriate criteria, such as hemodynamic stability and transfusion requirements are applied in patient selection. We report the case of a 36 year old man with infectious mononucleosis who had a spontaneous splenic rupture and who was successfully managed by splenectomy. Based on review of the literature, an approach to management of a spontaneously ruptured spleen secondary to IM is suggested.

INTRODUCTION

Infectious mononucleosis (IM)[b] is a common disease of young adults. The etiologic agent, the ubiquitous Epstein-Barr virus (EBV), is transmitted primarily through exchange of saliva but can also be transmitted with transfusion of blood and blood products. Primary infections with the virus tend to occur at an early age and are usually subclinical. Approximately 50 percent of pre-adolescent children seroconvert, that number climbing to 90-95 percent by adulthood [2]. Of the people that become primarily infected with EBV during the latter part of adolescence and young adulthood, 25-70 percent develop the clinical syndrome of infectious mononucleosis.

IM is defined by a clinical triad of fever, pharyngitis and lymphadenopathy as well as the presence of heterophil antibodies and atypical lymphocytes. It is a self-limited disease, with pharyngitis resolving in 7-10 days, fever in 7-14 days and lymphadenopathy by about 3 weeks. Splenomegaly is noted clinically in approximately 50 percent of patients, although by ultrasound, splenic enlargement has been shown to occur in as many as 100 percent of patients [3]. Approximately 90 percent of patients have hepatitis with mild elevations in serum transaminases [4].

Although the disease usually runs a benign course, approximately 0.1-0.5 percent of patients with IM suffer spontaneous splenic rupture [5]. Splenic rupture is typically heralded by abdominal pain. Signs of hypovolemia, such as tachycardia, orthostasis and syncope, may also be present. The presence of Kehr's sign (left shoulder pain), occurs in about 50 percent of splenic ruptures and is another clinical clue to alert the physician to the possibility of splenic rupture. Diagnosis can be made by abdominal ultrasound or CT scan.

In the face of hemodynamic instability, splenectomy is the treatment of choice. However, when the patient is hemodynamically stable, management becomes a source of debate. Though most authors still favor splenectomy, recently, several authors have

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[b] *Abbreviations:* IM, infectious mononucleosis; EBV, Epstein-Barr virus; SSR, spontaneous splenic rupture.

advocated non-operative management as a viable alternative [4, 6]. We report the case of a 36 year old previously healthy male with spontaneous splenic rupture and infectious mononucleosis. The patient presented with hemodynamic instability and was successfully managed surgically.

CASE REPORT

M.P., a 36 year old male with a history significant for peptic ulcer disease, presented to the Emergency Department with a four-day history of fever, chills, nausea, diarrhea and anorexia. On the day of admission, he noted the onset of acute abdominal pain localized to the epigastric area without any radiation. The pain was described as constant and severe. The patient experienced a syncopal episode that morning while attempting to raise himself from his bed, which led him to seek medical attention. The patient denied any history of recent trauma.

Upon his arrival at the Emergency Department, the patient complained of moderate abdominal pain. He had a temperature of 99.8°F, pulse of 101 and supine blood pressure of 80/38. He was noted not to have any evidence of pharyngitis or lymphadenopathy. His abdominal exam revealed tenderness to percussion and palpation with involuntary guarding in the upper abdomen and rebound tenderness localized to the epigastic region. His extremities were cool with faint distal pulses.

Laboratory data revealed a white blood cell count of 26,500 cells/ml with 30 percent atypical lymphocytes and a hematocrit of 32.7. Serum transaminases were slightly elevated with an alanine aminotransferase value of 294 u/l and an aspartate aminotransferase value of 172 u/l. Serum alkaline phosphatase was also elevated at 326 u/l.

The patient's atypical lymphocytosis, consistent with IM, combined with his clinical presentation of peritonitis and hypotension in the absense of a history of trauma, suggested the tentative diagnosis of a spontaneous splenic rupture. He was started on crystalloids for fluid replacement but was not given any blood transfusions. While awaiting a CT scan to confirm his diagnosis, the patient had several episodes of marked hypotension despite aggressive fluid replacement. Because of his hemodynamic instability, the decision was made to treat the patient surgically. At laparotomy, there was a large amount of fresh and clotted blood in the abdomen, and the spleen was large and congested. It had a 6 cm linear laceration involving the hilum, as well as a subcapsular hematoma on the lateral surface. The spleen was removed without incident and no other intra-abdominal pathology was noted.

Pathologic examination revealed an enlarged spleen, weighing 310 g. The splenic parenchyma showed marked infiltration with a heterogeneous population of small lymphocytes, activated lymphoid cells, immunoblasts, plasma cells and histiocytes. Marker studies demonstrated the majority of lymphoid cells to be of T-immunophenotype compatible with the clinical diagnosis of an active EBV infection. *In situ* hybridization for EBV with EBER oligonucleoprobes was positive for the presence of the virus.[c] A Monospot test obtained at the time of admission was later confirmed as positive for infectious mononucleosis.

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[c] EBERs are nonpolyadenylated RNA polymerase III transcripts that are abundant in EBV-infected cells. The EBER oligonucleoprobes are antisense probes that hybridize to EBER viral RNAs in clinical specimens. In situ hybridization with these probes is considered to be a very sensitive technique for detecting EBV immortalized cell lines due to the high copy number of the target within infected cells [7, 8].

DISCUSSION

Splenic involvement in IM is common: being clinically evident in 25-50 percent and detectable on ultrasound examination in as many as 100 percent of patients [3]. Grossly, the spleen appears boggy and edematous, often with lifting of the splenic capsule forming a subcapsular hematoma. Histologically, the red pulp appears congested with lymphocytic and atypical lymphoid cell infiltration. This infiltration extends to include the capsule, supporting trabeculae, and blood vessel walls of the spleen. As a result, the splenic capsule and fibrous support network may become fragmented and dissoluted, compromising the spleen's architecture and facilitating rupture.

Etiologic factors that may induce spontaneous splenic rupture include an acute increase in portal venous pressure such as that accompanying a Valsalva maneuver or any sudden compression of the enlarged spleen secondary to contraction of the diaphragm or abdominal wall [9]. The spleen is most vulnerable to rupture approximately 10-21 days after onset of clinical symptoms of IM when capsular and trabecular changes are most pronounced. In our case, the spleen spontaneously ruptured 4 days after the onset of clinical symptoms of IM. Early rupture, though unusual, has been reported as early as 3 days following the onset of symptoms [10].

Spontaneous splenic rupture secondary to IM was first reported in the literature by King in 1941 [11]. Five years later, Smith and Custer [12] demonstrated a mortality rate of approximately 30 percent. Although this mortality rate was based on only seven cases, it was so alarmingly high that it led physicians to view splenectomy as the treatment of choice for the disease. Other forms of treatment were mostly overlooked until more recently, when close examination of the cases revealed that the survival rate for "true" spontaneous splenic rupture (SSR) was higher than previously estimated [9]. Rutkow reviewed 107 cases of SSR reported in the world literature up to 1976 and suggested that only 18 of those cases were "true" spontaneous ruptures, occurring in patients with a well-established histologic and serologic diagnosis of IM. The other 89 cases, when examined with scrutiny, failed to fulfill criteria for true SSR in that 1) a history of traumatic injury could not be definitively ruled out; 2) the diagnosis of IM was not serologically confirmed; and 3) multi-system disease was present, suggesting the possibility of pathological as opposed to spontaneous rupture. Of the 18 true SSR cases, the survival rate was 100 percent. Though this estimated survival rate is more likely to be a closer approximation to the actual survival rate, it is, however, slightly elevated as compared with recent reports that have documented cases of sudden death due to true SSR fulfilling the above criteria [2, 13, 14]. Nevertheless, the higher estimated survival rate prompted interest in investigating spleen-sparing methods for treating SSR.

Most authors continue to advocate splenectomy as the treatment of choice in SSR [1, 10, 15-19]. They argue that there is no strong evidence that non-operative management is safe in the short-term or beneficial in the long-run. The sudden death of patients prior to any medical assistance illustrates the potential morbidity associated with non-surgical management [1]. They maintain that splenectomy is a safe procedure with low morbidity and mortality and that, most importantly, it is definitive. They cite the fact that, unlike the normal spleen which can readily repair itself after trauma, the diseased spleen does not possess the same reparative capabilities due to the changes in the basic framework of the organ. The capacity of the spleen to regain its immunologic function in patients managed nonoperatively after a spontaneous splenic rupture has yet to be determined.

In previous decades, splenectomy was unarguably the treatment of choice for splenic rupture because the spleen's immunologic function was obscure. It wasn't until 1952 when a landmark article by King and Schumaker [20] suggested that children who underwent splenectomies were at greater risk for developing sepsis, thus elucidating the entity

of post-splenectomy sepsis. Post-splenectomy sepsis is a potentially lethal complication of splenectomy with a mortality rate of 50 percent to 80 percent [21]. While the incidence of post-splenectomy sepsis is well-documented in the pediatric population [22], its incidence in teenagers and young adults, who are at greatest risk for IM, is less clear. O'Neal and McDonald [23] attempted to ascertain the risk of post-splenectomy sepsis in the asplenic young adult population by following a group of 256 asplenic adults aged 16-91 for a mean observation period of 45 months. The incidence of mortality from fulminant sepsis was 2.7 percent, a prevalence 540 times that of the normal adult population. This study was performed prior to the availability of the pneumococcal vaccine, which has considerably reduced the risk of sepsis secondary to pneumococcus. Since the vaccine is only between 60 percent to 100 percent effective, it has not eliminated the risk of pneumococcal sepsis [21]. More recent reports have estimated the risk of post-splenectomy sepsis to be less than 1 percent in patients who have undergone splenectomy for trauma [16, 24].

The importance of the spleen in immunologic function was further elucidated with studies showing that patients with splenectomies had reduced serum IgM levels, an inability to switch from IgM to IgG synthesis following secondary immunization [25] as well as a decreased response to various antigens [26]. The discovery of the spleen's role in immunologic function fostered changing attitudes favoring splenic conservation. Splenic conservation involves either splenorrhaphy or non-operative management. Successful splenorrhaphy has not been reported in IM-induced SSR rupture. There is one report of a successful splenorrhaphy after a traumatic splenic rupture in a patient with IM [27] in which a 3 cm laceration was repaired with an omental flap. More recently, an attempt at splenorrhaphy was made in a patient with SSR due to IM but was abandoned secondary to splenic disintegration during repair [28]. Many surgeons are unwilling to perform splenorrhaphy in IM due to the inherent fragility of the diseased spleen, which may render it more vulnerable to further hemorrhage following repair.

The advantages of non-operative management are that it eliminates the risk of post-splenectomy sepsis and saves the patient from potential perioperative complications. However, nonoperative management is not without risk. The patient may be prone to delayed splenic rupture and as a result, may require a longer period of follow-up with slower return to normal activities. The spleen can remain susceptible to rupture after all clinical, hematologic and serologic criteria document resolution of IM [9]. Johnson et al. [29] reported two patients with SSR occurring 4 and 7 weeks after the initial onset of IM. MacLean [30] reported a patient with recurrent spontaneous splenic rupture 69 days after hospitalization for splenic rupture secondary to IM. Since the length of time during which a patient with IM is at risk for splenic rupture remains uncertain, nonoperative management requires months of follow-up as well as restriction of activity for a 2-3 month period [9, 29]. This is often poorly tolerated in the young adult population.

Additionally, conservatively managed patients may require multiple blood transfusions with the attendant risk of viral transmissions. For viruses that can cause chronic, life-threatening infections, such as the hepatitis viruses and HIV, the results could be fatal. Fortunately, with the current screening of blood and blood products, that risk is minimized. For example, the risk of post-transfusion transmission of hepatitis C, which prior to anti-HCV screening in 1990 was estimated to be as high as 13 percent, is now as low as 0.1 percent [31]. Although the current estimation of the post-transfusion risk for transmission of viruses is markedly reduced, the inherent risk, albeit small, continues to persist.

There have been a total of 19 reported cases of successful non-operative management of patients with SSR and IM (Table 1), suggesting that non-operative management is justified in select patients. What criteria can be used to select the appropriate patients? In cases of adult blunt splenic trauma, Longo et al. [38] proposed parameters predicting successful

outcome as follows: (1) hemodynamic stability; (2) normal level of consciousness (3); under 50 years old; (4) transfusion requirements of less than 4 units of blood; (5) early resolution of splenic defects on imaging studies; and (6) rapid resolution of post-traumatic ileus. Some of the same parameters are useful in predicting a successful outcome in SSR. Few surgeons would advocate non-operative management in the face of hemodynamic instability or loss of consciousness. Since IM affects mostly the young adult population, age limitations are not useful. In comparing the 19 cases of successful outcomes of non-operative management to those that have failed, the most predictive variable appears to be the number of transfusions required to achieve hemodynamic stability.

Table 1. Successful non-operative therapy

Reference	Blood Units Transfused	Age (years)	Sex	Days of Hospitalization	Remarks
Ali, 1993 [13]	0	29	M	7	F/u* at 8 mo. revealed normal sized spleen with healed laceration
Evard, et al., 1993 [21]	0	18	F	13	
Farley et al., [1]	2	17	M	NA**	
	0	19	M	7	
	0	17	M	7	Elective splenectomy after 18 mo. for hypersplenism
Fleming, 1991 [32]	2	23	M	13	
Gauderer et al., 1989 [33]	2	17	M	14	
	0	16	F	14	Blunt abdominal trauma without sequelae 3 mo. after discharge
Gordon et al., 1995 [19]	0	22	M	10	Normal splenic architecture at 3 mo. f/u
Howman-Giles et al., 1978 [34]	NA	NA	NA	NA	
Johnson et al., 1981 [29]	Transfusion performed, No. units NA	14	M	NA	Stable amount of intrasplenic fluid collection at 4 mo. f/u
	0	14	F	NA	
	0	23	M	NA	
Peters & Gordon, 1986 [35]	8	28	M	NA	Hospital course complicated by SOB[†] and laryngospasm and intubation
Ruiz et al, 1990 [36]	0	17	F	NA	
Schuler & Filtzer, 1995 [37]	2	19	M	12	All patients symptom free at 1 year f/u
	1	22	F	6	
	1	21	M	6	

* F/u: follow-up; ** NA: not available, [†] SOB: shortness of breath.

In the cases reviewed, 16 of 19 patients who were successfully managed non-operatively required up to 2 units of blood to maintain hemodynamic stability. Ten required no transfusions [1, 13, 21, 19, 29, 33, 36], 2 required 1 unit [37] and four required 2 units [1, 32, 33, 37]. One patient required 8 units and subsequently developed shortness of breath

and laryngospasm requiring intubation [35], suggesting that non-operative management requiring numerous transfusions may lead to further complications.

In contrast, the available data show that most patients who failed non-operative therapy did so because of persistent hemodynamic instability requiring 5 or more units of blood (Table 2). The one exception is the patient reported by MacLean [30] who was initially successfully managed with nonoperative treatment. Upon admission, she stabilized hemodynamically with administration of 2 units of packed red blood cells and was discharged after 17 days with no complications. However, nine days later, she suffered blunt trauma to her abdomen at which point she developed recurrent left shoulder pain. This pain did not resolve and ultimately led to a laparotomy, which indicated delayed splenic rupture. This case suggests that the spleen may remain susceptible to delayed rupture for several months, though the exact length of time has yet to be determined. Thus, non-operational management should be reserved for patients who can tolerate strict restrictions on activity.

Table 2. Unsuccessful non-operative therapy

Reference	Blood Units Transfused	Age	Sex	Days Hospitalized	Remarks
Farley et al., 1992 [1]	NA*	17	F	NA	Splenectomy for hemodynamic instability 24 hrs after admission
	NA	28	M	NA	Splenectomy for hemodynamic instability 7 d. after admission
Gordon et al., 1995 [19]	7	20	M	NA	Splenectomy for hemodynamic instability 5 d. after admission
	5	20	M	NA	Splenectomy for hemodynamic instability 4 hrs after admission
	18	57	M	NA	Splenectomy for hemodynamic instability 36 hrs after admission
McLean et al., 1987 [30]	2	14	F	7	Initially managed with 2 units pRBCs.** Readmitted twice for RUQ[†] pain. Splenectomy 69 d. after presentation
Vezina et al., 1984 [39]	NA	20	M	NA	Splenectomy 1 week after admission
Vitello, 1986 [17]	6	16	M	NA	Splenectomy for hemodynamic instability

* NA: not available; ** pRBCs: packed red blood cells; † RUQ: Right upper quadrant

SUMMARY

Spontaneous splenic rupture is the most common fatal complication of IM. A high index of suspicion is necessary on the part of the physician to diagnose the disease and initiate appropriate management. Although splenectomy is still the treatment of choice for the majority of patients with spontaneous splenic rupture, carefully selected patients may benefit from non-operative management. Previous reports have failed to state how patients were selected for non-operative management. We propose selecting those patients with

SSR who require no more than 2 units of blood to maintain hemodynamic stability. Any such guidelines, however, would need to be investigated with a retrospective study to further analyze patients treated both surgically and non-operatively. Establishment of such guidelines for decision making could facilitate recognition of the point at which non-operative therapy fails and surgical intervention is indicated.

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